CLAIMS

1. A method of altering the substrate specificity of phosphoinositide-dependent protein kinase 1 (PDK1) wherein the said PDK1 is exposed to an interacting polypeptide which comprises the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr wherein Zaa represents a negatively charged amino acid residue.

2. A preparation comprising PDK1 and an interacting polypeptide which comprises the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr wherein Zaa represents a negatively charged amino acid residue characterised in that the said preparation is substantially free of polypeptides with which PDK1 is present or associated in a cell in which it is naturally found other than a said interacting polypeptide or a substrate for PDK1.

3. PDK1 derivable by the method of claim 1 wherein the said PDK1 has altered substrate specificity and is substantially free of polypeptides with which PDK1 is present or associated in a cell in which it is naturally found other than a said interacting polypeptide or a substrate for PDK1.

4. A method of phosphorylating a residue corresponding to the underlined residue in a substrate polypeptide with an amino acid sequence corresponding to the consensus sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Ser/Thr-Phe/Tyr wherein (1) a preparation comprising PDK1 and a polypeptide which comprises the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr or (2) PDK1 derivable by a method of altering the substrate specificity of phosphoinositide-dependent protein kinase 1 (PDK1) wherein the said PDK1 is exposed to a polypeptide which

comprises the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr is used wherein Zaa represents a negatively charged amino acid residue.

5. A method of phosphorylating PRK2 wherein the said PRK2 is exposed to PDK1.

6. A preparation comprising PDK1 and PRK2 in the substantial absence of other proteins or cellular components.

7. A method of identifying a compound that modulates the activation and/or phosphorylation of PRK2 by PDK1 wherein the activation and/or phosphorylation of PRK2 by PDK1 is measured in the presence of more than one concentration of the compound.

8. A method of identifying a compound that modulates the activity of PDK1 wherein the said PDK1 is exposed to the said compound in the presence of a polypeptide comprising the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr wherein Zaa represents a negatively charged amino acid residue.

9. A method according to claim 8 comprising the step of measuring the activity of the said PDK1 in the presence of more than one concentration of the compound wherein the said PDK1 is or has been exposed to a polypeptide which comprises the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr.

10. A method according to claim 8 or 9 wherein the said compound is capable of modulating the interaction between a polypeptide which

comprises the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr and PDK1.

11. A method of identifying a compound that is capable of altering the substrate specificity of PDK1 wherein the ability of the said PDK1 to phosphorylate a residue corresponding to the underlined residue in a polypeptide with an amino acid sequence corresponding to the consensus sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Ser/Thr-Phe/Tyr is measured, and is increased in the presence of the said compound

12. A method of altering the substrate specificity of phosphoinositide-dependent protein kinase 1 (PDK1) wherein the said PDK1 is exposed to a compound identified or identifiable by the method of claim 11.

13. A method of identifying a compound that is capable of mimicking the effect of a 3-phosphoinositide, for example PtdIns(3,4,5)P_3 or PtdIns(3,4)P_2, on the PDK1 or PDK2 activity of (1) a PDK1 which has altered substrate specificity derivable by the method of claim 1 or 12 or (2) a preparation according to claim 2, 24 or 25, the method comprising determining whether said compound activates a said PDK1 or preparation so that it can phosphorylate a suitable substrate, the activation by said compound being in the absence of a 3-phosphoinositide.

14. A protein kinase derivable from mammalian brain wherein said protein kinase is capable of phosphorylating a residue corresponding to the underlined residue in a polypeptide with an amino acid sequence corresponding to the consensus sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Ser/Thr-Phe/Tyr, for example Ser473 of PKBα in the presence of PtdIns(3,4,5)P_3, wherein the said protein kinase is eluted from Heparin-

Sepharose by at least 0.75M NaCl at pH 7.5 and is capable of binding to an antibody reactive with PDK1.

15. A polypeptide which comprises the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr wherein said polypeptide is not full-length PRK2, PRK1 or PKCς and wherein Zaa is a negatively charged amino acid that is not phosphoserine or phosphothreonine.

16. A polypeptide consisting essentially of residues 51 to 404 of PDK1 or a fusion of a polypeptide consisting essentially of residues 51 to 404 of PDK1.

17. A polynucleotide encoding a polypeptide as defined in claim 15 or 16.

18. A recombinant polynucleotide suitable for expressing a polypeptide as defined in claim 15 or 16.

19. A host cell comprising a polynucleotide as defined in claim 18.

20. A method of making a polypeptide as defined in claim 15 or 16 the method comprising culturing a host cell as defined in Claim 19 which expresses said polypeptide and isolating said polypeptide.

21. A polypeptide obtainable by the method of Claim 20.

22. A cell containing a recombinant nucleic acid suitable for expressing PDK1 and a recombinant nucleic acid suitable for expressing a polypeptide comprising the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr.

23. A method according to claim 1 wherein the said PDK1 is exposed to the said interacting polypeptide in a cell as defined in claim 22.

24. A method of making a preparation comprising PDK1 and an interacting polypeptide comprising the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr wherein PDK1 and the said interacting polypeptide are co-expressed in a cell as defined in claim 22.

25. A method according to claim 24 wherein the said PDK1 and the said interacting polypeptide are separated from other components of the said cell.

26. A preparation obtainable by the method of claim 24 or 25.

27. A compound identifiable or identified by the method of any one of claims 8 to 13.

28. A compound as defined in claim 27 for use in medicine.

29. Use of a compound as defined in claim 27 in the manufacture of a medicament for the treatment of a patient in need of modulation of the insulin signalling pathway and/or PDK1, PDK2 or PRK2 signalling.

30. A polypeptide which comprises the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr or a polypeptide consisting essentially of residues 51 to 404 of PDK1 or a fusion of a polypeptide consisting essentially of residues 51 to 404 of PDK1 wherein Zaa represents a negatively charged amino acid residue for use in medicine.

31. Use of a polypeptide as defined in claim 30 in the manufacture of a medicament for the treatment of a patient in need of modulation of the insulin signalling pathway and/or PDK1, PDK2 or PRK2 signalling.

32. A kit of parts useful in carrying out a screening method according to any one of claims 8 to 13 wherein the kit comprises PDK1 and a polypeptide comprising the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr wherein Zaa represents a negatively charged amino acid residue.

33. A method of making a preparation that comprises PDK1 and a polypeptide which comprises the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr wherein substantially pure PDK1 is mixed with a substantially pure polypeptide which comprises the amino acid sequence Phe/Tyr-Xaa-Xaa-Phe/Tyr-Zaa-Phe/Tyr.